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(12) The surfactant concentrations are substantially above the critical micelle concentrations.[2,9,10] For models M_c and M_d, higher concentrations had to be used in order to differentiate the model-driven reactions from buffer hydrolysis; see Table I.
(13) This parallelism probably originates in greater bonding between surfactant functionality and substrate carbonyl at the cleavage reaction transition states with the more reactive surfactants: greater bond formation results in more accelerated cleavage *and* more stereochemical information transfer (i.e., greater stereoselectivity).
(14) Interestingly, cleavages mediated by the models also favor LL-I over DL-I. However, substantial stereoselectivity ($k_\psi^{LL}/k_\psi^{DL} > 2$) is encountered only with S_b–S_e. Note that the 1.5-fold stereoselectivity exhibited by M_d is expressed at 0.02 M, a concentration five times greater than that employed with S_d. At 4×10^{-3} M, enhancement by M_d is only ~50%, relative to buffer rates.
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Received December 26, 1978

Stereoselective Synthesis of *threo*-3-Hydroxy-2-methylcarboxylic Acids Using Alkoxyalkyl Propionates

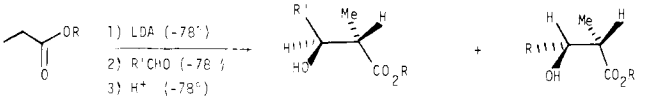
Sir:

Among the most fundamental and significant synthetic reactions is carbon–carbon bond formation via aldol or related processes (Scheme I).[1] In recent years, a considerable amount of activity has ensued with the emphasis focusing on stereoselectivity accompanying the C–C bond-forming step. In this regard, studies have been reported[2] involving the effects of steric bulk, solvent, nature of the metal, kinetic vs. thermodynamic control, and the geometry of the enolate species. Closely related to this problem is the stereoselective formation of β-hydroxy acids, readily prepared from lithio enolates of simple carboxylic esters (Scheme I, R = *O*-alkyl) and carbonyl compounds.[3] Heathcock[4] has recently reported routes to *erythro*- and *threo*-β-hydroxy acids by use of bulky α-silyloxy enolates (Scheme I, R = $-C(Me)_2OSiMe_3$) or chromium(II)-mediated addition of allylic halides to aldehydes. Mulzer,[5] using ester enolates, was able under equilibrating conditions to form, in certain instances, high ratios of *threo*-β-hydroxy-α-alkylcarboxylic acids.

We now report some preliminary results of a study in which various alkoxyalkyl propionates, **1**, via their lithio enolates give rise to high threo:erythro ratios of 2-methyl-3-hydroxycarboxylic acids **2**. It appears that no serious effort has been reported which considers the effect of internal lithium chelation in the enolate *prior to addition* to the carbonyl component. Table I describes the result of this effect with the simple methyl ester of propionic acid as a control. It can be seen that generating the *Z* lithio enolate (THF, −78 °C)[2a] of methyl propionate and addition (−78 °C) of isobutyraldehyde gives a 1.2:1 threo:erythro ratio of **2**. However, this ratio climbs to 8.5–10:1 when various alkoxyalkyl esters are metalated and alkylated under identical conditions. In the case of the MEM ester (footnote *e*, Table I), which led to a 10:1 ratio of diastereomeric esters, produced exclusively the threo ester when isobutyraldehyde was introduced into the enolate solution at −98 °C. This implies that even greater stereochemical control is attainable at lower alkylation temperatures. This was not to be the case, however, with acetaldehyde addition which gave essentially 2:1 threo:erythro products at −98 °C. The lithium enolates of the alkoxyalkyl esters were trapped with trimethylsilyl chloride and shown (^{1}H NMR, VPC) to be a single (>98%) geometric isomer which we assigned as *E* in accordance with previous results obtained by others.[2,6] With regard to the kinetic and thermodynamic nature of the preponderant threo product, we can only say at this time that there was no change in product ratio after 20 h at −78 °C. Unfortunately, side reactions occur in the adduct above −50 °C which precluded examination of the product ratios at higher temperature. For optimum yield of product, the reactions should be quenched, after 5–10 min at −78 °C, with acetic acid (1.05 equiv) in THF.

The major point of interest in these results appears to be the generality with which coordinating groups increase the selectivity of the 3-hydroxy-2-methyl acids, regardless of the nature of the alkyoxyalkyl group. It can be assumed at this time that the in situ generation of a bulky group in the enolate provides the steric control necessary for enhanced stereo-

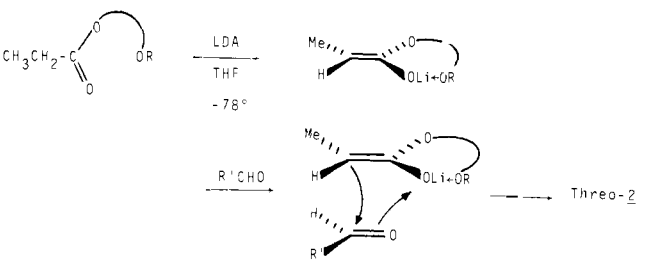
Table I. Stereoselectivity Using Alkoxyalkyl Ester Enolates



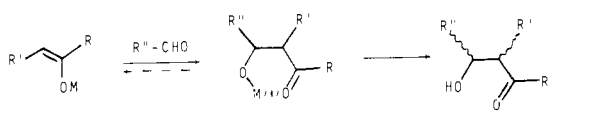
1 threo-2 erythro-2

R	R′CHO	ratio[a]	% threo[b,c]	% erythro
Me	*i*-PrCHO	1.2:1	55	45
CH_2OMe[d]	*i*-PrCHO	8.5:1	90	10
$CH_2O(CH_2)_2OMe$[e]	*i*-PrCHO	10:1	91	9
$C(CH_3)OEt$[f]	*i*-PrCHO	10:1[g]	91	9
Me	CH_3CHO	1.3:1	57	43
CH_2OMe	CH_3CHO	2:1	67	33
Me	PhCHO	1.2:1	55	45
$CH_2O(CH_2)_2OMe$	PhCHO	3:1[g]	75	25

[a] Determined by high pressure liquid chromatography (Waters 244 system) using 1-ft micro-Porasil column and eluted with $CHCl_3$–CH_3CN, 99:1, at a flow rate of 3 mL/min. [b] Assigned by ^{1}H NMR spectrum of C-2, C-3 protons and couplings (J = 7 Hz for *threo*-**2** and 4 Hz for *erythro*-**2**). [c] Chemical yields ranged from 84 to 98% for total product. [d] Prepared from propionic acid, potassium *tert*-butoxide, and chloromethylmethyl ether in anhydrous ether, bp 125–126 °C (atm), 80%. [e] Prepared as in *d* using 1.0 equiv of methoxyethoxy chloromethyl ether (MEM-Cl, Aldrich), distilled by Kugelrohr apparatus (0.05 Torr, trap distillate at −78 °C), 82%. [f] Prepared from propionic acid, excess methylvinyl ether, and a trace of toluenesulfonic acid (1 h, 25 °C), bp 37–38 °C (20 mm, 85%). [g] Product ratio determined after hydrolysis of ester.



Scheme I



R = alkyl, aryl, OAlkyl
R',R" = alkyl, aryl
M = Li, Na, K, MgX, ZnX

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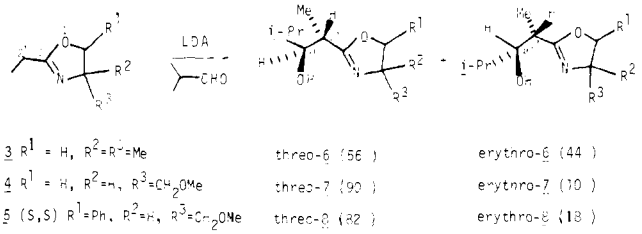
chemical control. From a synthetic point of view, these esters are readily purified by chromatography and the carboxylic acid obtained by simple acid hydrolysis (3 N HCl, THF, 25 °C, 12 h).

To further test the efficacy of internal lithium chelation toward enhanced threo-erythro selectivity, the 2-ethyl oxazolines **3**-**5**[7] were examined. Metalation of **3** (−78 °C, THF) followed by introduction of isobutyraldehyde gave diastereomeric **6** as a 56:44 mixture. However, when methoxy-substituted oxazoline **4** was similarly treated, a 9:1 ratio of threo:erythro adducts **7** was obtained.[8] Thus, the internal lithium chelation in lithiated oxazolines provides the necessary steric parameters for enhanced selectivity during C-C bond formation along with a high degree of selectivity in the deprotonation step.[9,10]

When the chiral, nonracemic oxazoline **5** was metalated and



3 R^1 = H, R^2=R^3=Me — threo-6 (56) — erythro-6 (44)
4 R^1 = H, R^2=H, R^3=CH_2OMe — threo-7 (90) — erythro-7 (10)
5 (S,S) R^1=Ph, R^2=H, R^3=CH_2OMe — threo-8 (82) — erythro-8 (18)

treated (−98 °C, THF) with isobutyraldehyde, four nonracemic diastereomers in the ratio of 18.3:1:2.4:2.2 were observed (LC). The four products were identified as 82% *S,S* and *R,R* enantiomers and 18% *S,R* and *R,S* enantiomers. The *S,S* enantiomer was present as 75% of the total mixture and could be readily isolated by preparative medium-pressure chromatography. The high selectivity observed is in contrast to a much lower selectivity (~1.5:1) reported[11] using the chiral 2-methyloxazoline **5** (methyl in place of the 2-ethyl group) and aldehydes to furnish 3-hydroxyalkanoic acids. The presence of C-2′,C-3′ substitution in **8** undoubtedly creates a more demanding steric array in the transition state. Since these oxazolines are easily hydrolyzed to the carboxylic acids,[12] a route is now available for the acquisition of *threo*-(2*S*,3*S*)-2-alkyl-3-hydroxy acids. Further studies involving internally chelated lithio enolates as reagents for stereoselective C-C bond-forming reactions are continuing.

Acknowledgment. Support for this work was furnished by the National Science Foundation.

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(8) The oxazolines were hydrolyzed to the corresponding known acid[4] to confirm the threo-erythro assignment. Furthermore, the ^1H NMR spectra for **6**-**8** showed J = **7** Hz for C_2'-C_3' protons in the threo isomer and J = 2.8 Hz for C_2'-C_3' protons in the erythro isomer. This is in agreement with previous observations.[1]
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(10) It has been noted during this work that the stereoselectivity increases as the temperature of alkylation decreases. Thus, the stereoselectivity is not totally dependent upon the *E* or *Z* enolate ratio of the preformed enolate, but also on the nonbonded interactions in the transition state (cf. ref 2b, 5, and 7).
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Photoionization by Green Light

Sir:

In a recent communication[1] we showed that the photoionization of aminoperylene by green light (λ = 5300 Å) directly followed laser light intensity in the range 30-150 mJ/pulse. Some concern[2] has recently been exhibited with regard to the interpretation of the intensity dependence; attention was drawn[2] to another system where the yield of photoionization did not follow simple patterns. The system quoted, pyrene in anionic micellar solution, was not that reported in our communication,[1] although we have studied this system successfully a number of years ago[3-5] and find different mechanisms for these quite distinct systems. However, to avoid ambiguity we present two additional areas of experimental data: (a) an extension of our intensity data and (b) low intensity photoionization as measured by the SF_6 method.

Figure 1 shows the dependence of the yield of photoionization on the laser intensity, in which we present our original data together with an extension to lower intensities. An intensity range of 8-150 J/(cm^2/pulse) was covered. The data are linear and extrapolate through the origin. Photoionization of pyrene in NaLS micelles shows quite different behavior.[2,3] It is difficult to compare the aminoperylene data with the reported pyrene data,[2] in particular as the cross section of the laser beam and hence the irradiated volume are not given. However the aminoperylene data (Figure 1) again supported one-photon photoionization of aminoperylene in NaLS micelles.

To achieve extremely low light intensities we have photoionized aminoperylene in NaLS micelles with light (λ = 5300 Å) of 1-mW intensity, i.e. much lower than that used in the laser work. This light was obtained by passing the whole beam of a 450-W xenon lamp through an f 3.5 Bausch and Lomb monochromator which also had a filter at the exit slit. Solutions containing 5×10^{-5} M aminoperylene in 2×10^{-2} M NaLS together with O^2 ($[O_2] = 1.4 \times 10^{-4}$ M) and SF_6 ($[SF_6] = 1.3 \times 10^{-4}$ M) were photolyzed with this light. Fluoride ion was produced and measured on a fluoride sensitive electrode; no F^- was produced in absence of aminoperylene, or if NaLS was replaced by nonionic Igepal micelles. F^- results from the capture of e_{aq}^- produced in photoionization of aminoperylene by giving SF_6 $6F^-$ ions.[6] Excitation of aminoperylene leads to the excited singlet state and subsequently to the excited triplet. No reaction of the excited singlet or triplet state with SF_6 in SF_6 saturated solutions would be detected. The inclusion of O_2 which reacts at a diffusion-controlled rate with excited states of aminoperylene protects against two-photon photoionization of aminoperylene from the triplet state. Absorption by the foregoing solution of 0.31×10^{18} and 0.72×10^{18} quanta of light (λ = 5300 Å) produced 5.8×10^{16} and 12.0×10^{16} F^-, respectively. From the known rate constants for reaction of e_{aq}^- with O_2 ($k = 1.80 \times 10^{10}$ M^{-1} S^{-1}) and SF_6 ($k = 1.65 \times 10^{10}$ M^{-1} S^{-1}), and the fact that e_{aq}^- produces $6F^-$, the $[e_{aq}^-]$'s produced in photolysis are 2.1×10^{16} and 4.4×10^{16} molecules, respectively. The quantum yield for photoionization is thus 6.0×10^{-2}.

The above experiments support the observation of one-photon photoionization of aminoperylene in NaLS micelles

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